

L3 ANSWER 11 OF 31 MEDLINE on STN  
 AN 2002312092 MEDLINE  
 DN 22038074 PubMed ID: 12042430  
 TI The glutamate carboxypeptidase gene II (C>T) polymorphism does not affect **folate** status in the Framingham Offspring cohort.  
 AU Vargas-Martinez Carolina; Ordovas Jose M; Wilson Peter W; Selhub Jacob  
 CS The Nutrition and Genomics Laboratory, Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging, Tufts University, Boston, MA 02111, USA.. cvargas@hnrc.tufts.edu  
 NC HL 54776 (NHLBI)  
 SO JOURNAL OF NUTRITION, (2002 Jun) 132 (6) 1176-9.  
 Journal code: 0404243. ISSN: 0022-3166.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200206  
 ED Entered STN: 20020611  
 Last Updated on STN: 20020626  
 Entered Medline: 20020625  
 AB **Glutamate carboxypeptidase II (GCP II**  
 ) hydrolyzes polyglutamyl folates before their absorption. Recently, a 1561 C>T polymorphism in the **GCP II** gene was reported to be associated with lower **folate** and higher homocysteine plasma concentrations in a small (n = 75) selected elderly population. In this study, we examined the effect of this polymorphism in 680 men and 644 women attending the fifth examination of the Framingham Offspring Study. At the time of sample collection, subjects were not taking any supplements and were not exposed to food **folate** fortification. **GCP II** genotypes were determined by allelic discrimination using Taqman probes. In the population as a whole, this mutation was not associated with lower plasma **folate** level or with elevated plasma homocysteine. In men, plasma **folate** concentrations were higher in carriers of the T allele compared with those homozygotes of the wild-type allele (P < 0.05), whereas in women **folate** concentrations did not differ between genotypes (P = 0.8). In its relationship to plasma **folate**, this mutation exhibited a weak interaction with age and gender only in older women (P = 0.05). Overall, our data show that the **GCP II** C1561T polymorphism is not a determinant of plasma **folate** or total homocysteine concentrations in this large cohort of participants from the Framingham Offspring Study.

L3 ANSWER 7 OF 31 MEDLINE on STN  
 AN 2003177166 MEDLINE  
 DN 22581965 PubMed ID: 12694331  
 TI Genetic determinants of the homocysteine level.  
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 CS Department of Medicine III, Division of Nephrology and Dialysis and  
 Institute of Medical and Chemical Laboratory Diagnostics, University of  
 Vienna, Vienna, Austria.. Gere.Sunder-Plassmann@univie.ac.at  
 SO KIDNEY INTERNATIONAL. SUPPLEMENT, (2003 May) (84) S141-4. Ref: 22  
 Journal code: 7508622. ISSN: 0098-6577.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW LITERATURE)  
 LA English  
 FS Priority Journals  
 EM 200307  
 ED Entered STN: 20030417  
 Last Updated on STN: 20030717  
 Entered Medline: 20030716  
 AB Elevated total homocysteine (tHcy) plasma concentrations indicate  
**folate** and/or vitamin B12 deficiency and are associated with  
 cardiovascular disease and neural tube defects. Evidence has accumulated  
 that **folate**-, vitamin B12-, and Hcy-metabolism are under genetic  
 control. Because Hcy metabolism is impaired in renal failure, MTHFR 677  
 C>T, GCP2 1561C>T, RFC1 80G>A, and TCN2 776G>C may further aggravate  
 hyperhomocysteinemia in these patients. The most consistent effect on  
 tHcy plasma concentrations is observed for 677C>T of MTHFR, whereas GCP2,  
 RFC1, and TCN2 polymorphisms show no major effect on tHcy concentrations.  
 Much is yet to be learned about the impact of genetic variants on tHcy  
 levels, human diseases, the genetic-nutrient interactions, as well as the  
 pharmacogenetic consequences in Hcy and vitamin metabolism.

L3 ANSWER 15 OF 31 MEDLINE on STN  
 AN 2001073218 MEDLINE  
 DN 20545101 PubMed ID: 11092759  
 TI **Glutamate carboxypeptidase II**: a  
 polymorphism associated with lower levels of serum **folate** and  
 hyperhomocysteinemia.  
 AU Devlin A M; Ling E H; Peerson J M; Fernando S; Clarke R; Smith A D;  
 Halsted C H  
 CS Department of Internal Medicine, University of California, Davis, CA  
 95616, USA.  
 NC DK-35747 (NIDDK)  
 DK-45301 (NIDDK)  
 SO HUMAN MOLECULAR GENETICS, (2000 Nov 22) 9 (19) 2837-44.  
 Journal code: 9208958. ISSN: 0964-6906.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-AF176574  
 EM 200101  
 ED Entered STN: 20010322  
 Last Updated on STN: 20010322  
 Entered Medline: 20010103  
 AB Low blood **folate** levels result in hyperhomocysteinemia, which  
 has been associated with increased risk for cardiovascular disease, neural  
 tube defects and cognitive deficits. Intake of dietary folates is the  
 chief determinant of blood **folate** levels. Molecular defects in  
 the intestinal absorption of dietary folates that precipitate low blood  
**folate** levels and hyperhomocysteinemia have not been investigated  
 previously. Dietary folates are a mixture of polyglutamylated folates  
 which are digested to monoglutamyl folates by the action of  
 folylpoly-gamma-glutamate carboxypeptidase (FGCP), an enzyme that is  
 anchored to the intestinal brush border membrane and is expressed by the  
 glutamate carboxypeptidase II (**GCPII**) gene. We cloned  
**GCPII** cDNA from human intestine and identified both a full-length  
 transcript and a 93 bp shorter transcript lacking exon 18, consistent with  
 the presence of a splice variant. In addition, we identified an H475Y  
 polymorphism in **GCPII** in DNA samples from a healthy Caucasian  
 population (n = 75). We found that membranes of transfected COS-7 cells  
 expressing the H475Y variant **GCPII** cDNA had 53% less FGCP  
 activity than did cells expressing wild-type **GCPII**. The  
 presence of the H475Y **GCPII** allele was significantly associated  
 with lower **folate** and higher homocysteine levels in this  
 population. These data suggest that the presence of the H475Y  
**GCPII** allele impairs the intestinal absorption of dietary folates,  
 resulting in relatively low blood **folate** levels and consequent  
 hyperhomocysteinemia.

L3 ANSWER 22 OF 31 MEDLINE on STN  
 AN 1999057588 MEDLINE  
 DN 99057588 PubMed ID: 9838072  
 TI Mapping, genomic organization and promoter analysis of the human prostate-specific membrane antigen gene.  
 AU O'Keefe D S; Su S L; Bacich D J; Horiguchi Y; Luo Y; Powell C T; Zandvliet D; Russell P J; Molloy P L; Nowak N J; Shows T B; Mullins C; Vonder Haar R A; Fair W R; Heston W D  
 CS Urologic Oncology Research Laboratory, Molecular Pharmacology and Therapeutics Division, Sloan-Kettering Institute for Cancer Research, Box 334, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY 10021, USA.  
 NC DK/CA 47650 (NIDDK)  
 SO BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Nov 26) 1443 (1-2) 113-27. Journal code: 0217513. ISSN: 0006-3002.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-AF007544  
 EM 199902  
 ED Entered STN: 19990216  
 Last Updated on STN: 20000303  
 Entered Medline: 19990204  
 AB Prostate-specific membrane antigen (PSMA) is a 100 kDa type II transmembrane protein with **folate** hydrolase and NAALAdase activity. PSMA is highly expressed in prostate cancer and the vasculature of most solid tumors, and is currently the target of a number of diagnostic and therapeutic strategies. PSMA is also expressed in the brain, and is involved in conversion of the major neurotransmitter NAAG (N-acetyl-aspartyl glutamate) to NAA and free glutamate, the levels of which are disrupted in several neurological disorders including multiple sclerosis, amyotrophic lateral sclerosis, Alzheimer's disease and schizophrenia. To facilitate analysis of the role of PSMA in carcinoma we have determined the structural organization of the gene. The gene consists of 19 exons spanning approximately 60 kb of genomic DNA. A 1244 nt portion of the 5' region of the PSMA gene was able to drive the firefly luciferase reporter gene in prostate but not breast-derived cell lines. We have mapped the gene encoding PSMA to 11p11-p12, however a gene homologous, but not identical, to PSMA exists on chromosome 11q14. Analysis of sequence differences between non-coding regions of the two genes suggests duplication and divergence occurred 22 million years ago.

L3 ANSWER 21 OF 31 MEDLINE on STN  
AN 1999236452 MEDLINE  
DN 99236452 PubMed ID: 10221263  
TI Characterization of the enzymatic activity of PSM: comparison with brain  
NAALADase.  
AU Tiffany C W; Lapidus R G; Merion A; Calvin D C; Slusher B S  
CS Guilford Pharmaceuticals, Inc., Baltimore, Maryland 21224, USA.  
SO PROSTATE, (1999 Apr 1) 39 (1) 28-35.  
Journal code: 8101368. ISSN: 0270-4137.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199905  
ED Entered STN: 19990607  
Last Updated on STN: 20000303  
Entered Medline: 19990527  
AB BACKGROUND: The prostate cancer marker prostate-specific membrane antigen  
(PSM) is highly homologous to the brain enzyme N-acetylated alpha-linked  
acidic dipeptidase (NAALADase). NAALADase is known to cleave terminal  
carboxy glutamates from both the neuronal peptide N-  
acetylasparylglutamate (NAAG) and **folate** polyglutamate. In  
this report, we compare the NAAG hydrolyzing activity of NAALADase and the  
prostate enzyme PSM. METHODS: Using a NAAG hydrolytic radioenzymatic  
assay, we compared the pharmacological and kinetic properties of the brain  
and prostate enzymes. RESULTS: Eight normal prostate tissues from  
different species exhibited NAAG hydrolyzing activity. Among 14 cancer  
cell lines examined, activity was observed in human LNCaP, PC-82, and rat  
Dunning G and AT-1 cells. Brain exhibited membrane-localized activity  
exclusively, while the prostate enzyme had activity in both membrane and  
cytosolic fractions. The only observed pharmacological difference was the  
sensitivity to their putative substrates, **folate** polyglutamate  
and NAAG. Kinetically, the soluble form of the prostate enzyme had two  
catalytic sites, while the membrane-bound form exhibited single site  
kinetics with a lower Vmax than the brain enzyme, which may suggest a less  
active hydrolase in the prostate. CONCLUSIONS: The brain enzyme NAALADase  
and the prostate enzyme PSM are remarkably similar. The importance of the  
differences in substrate specificities and kinetic parameters remains to  
be elucidated.